REMARKS

Claims 1-5 and 8 are under examination in the present case. Each of these claims is rejected under 35 U.S.C. § 112, second paragraph. The rejections are addressed below.

Support for the amendments

Support for the amendments is found throughout the specification; for example, support for the amendment of claim 1, which now recites "Alzheimer's disease-related cognitive impairment" is found at page 26, lines 3-26; and at Figure 8. Support for the amendment of claims 4 and 5, which now recite "genotype of said patient sample with respect to apoE4 allele " is found at page 6, lines 12-18; at page 6, lines 32-34; at page 10, lines 10-19; and at page 26, lines 27-31.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-5 and 8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

The Examiner rejects independent claim 1, and dependent claims 2 and 3, as indefinite for reciting "beneficial effects." In accordance with the Examiner's suggestion, the amended claims now recite "Alzheimer's disease-related cognitive impairment is responsive to treatment."

The Examiner rejects claims 4 and 5 as indefinite. The Examiner asserts that the claims are indefinite in specifying the patient's group placement and treatment. The claims have been amended to clarify that the genotype of the patient sample (i.e., the patient's apoE4 allele) is used to compare the effects of the drug on patients having different apoE4 genotypes. As shown in Figure 8, apoE4 genotype is useful in comparing the effects of a drug in a clinical trial. The indefiniteness rejections may be withdrawn.

Rejection under doctrine of obviousness-type double patenting

Claims 1-5 and 8 are rejected as being unpatentable over claims 1-4 of U.S. Patent No. 5,935,781 ('781 patent). To overcome this rejection, Applicant will submit a terminal disclaimer in compliance with 37 C.F.R. 1.321(c) once notice of otherwise allowable subject matter is received.

CONCLUSION

A marked-up version indicating the amendments to the claims, and a clean version of all pending claims is enclosed.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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Version of Claims Showing Changes Made

1. (Twice Amended) A method for the identification of human subjects [to be responsive to a cholinomimetic drug, said subjects,] having Alzheimer's disease responsive to treatment with a cholinomimetic drug, said method comprising determining the presence of *apoE4* gene alleles in said subject, wherein the absence of an *apoE4* gene allele in a biological sample of said subject [indicates a predisposition to receive beneficial effects from] identifies said subject as a subject whose Alzheimer's disease-related cognitive impairment is responsive to treatment with a cholinomimetic drug.

4. (Twice Amended) A method for genotyping [identifying] a patient sample with respect to apoE4 allele in a clinical trial of a drug for the treatment of cognitive impairments, said method comprising:

(a) identifying a patient already diagnosed with said cognitive impairments, or as being predisposed to acquire or to be at risk for said cognitive impairments; and

(b) determining the presence of *apoE4* gene alleles in said patient, wherein [absence of an *apoE4* allele places the patient into a group that either receives or does not receive] the genotype of said patient sample with respect to apoE4 allele [said drug for said] in a clinical trial of said drug allows the effects of said drug to be compared according to apoE4 genotype.

5. (Twice Amended) A method for genotyping [identifying] a patient sample with respect to apoE4 allele in a clinical trial of a drug for the treatment of Alzheimer's disease, said method comprising:

(a) identifying a patient already diagnosed with said Alzheimer's disease or as being predisposed to acquire or to be at risk for said disease; and

(b) determining the presence of *apoE4* gene alleles in said patient, wherein the genotype of said patient sample with respect to apoE4 allele [an absence of an *apoE4* allele places the patient into a subgroup] in said clinical trial of a drug for the treatment of said

Alzheimer's disease allows the effects of said drug to be compared according to apoE4 genotype.